Interview Summary

An interview with Examiner Minnifield was conducted via telephone on November 7, 2001. The enablement rejection set forth in the Office Action mailed August 28, 2001, was discussed. Rebecca McNeill (Reg. No. 43,796) and Todd Rands (Reg. No. 46,249) participated in the interview. The Examiner indicated that additional evidence in support of enablement would be considered and may be sufficient to overcome the rejection.

Enablement Rejection

The Examiner rejects claims 16-20 under 35 U.S.C. § 112, first paragraph, as allegedly not enabled by the specification. According to the Examiner, the claims are directed to a method for treating rheumatoid arthritis in a human subject comprising administering to the subject IL-12 an antagonist (antibody or antibody fragment immunoreactive with IL-12). The specification, she alleges, teaches that IFN-γ is implicated in the development, exacerbation, and/or recurrence of autoimmune conditions and that IFN-γ is associated with multiple sclerosis, IDDM, and rheumatoid arthritis. The Examiner maintains the position that while examples on IDDM and multiple sclerosis are set forth in the specification, it does not provide sufficient guidance for the treatment of rheumatoid arthritis.

Applicants contend that the presently claimed invention is fully enabled by the specification. As the Examiner notes, the specification enables one of skill in the art to make and use IL-12 antagonists. Specifically, the Examiner notes the Examples using IL-12 antagonists to treat IDDM and multiple sclerosis. Moreover, as Applicants discussed with the Examiner during their recent interview, multiple sclerosis works by a

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000

mechanism that is known to be similar to rheumatoid arthritis. Specifically, both conditions are aggravated by TNF-α. The specification specifically discloses this fact. "Both IFN-γ and TNF-α have been associated with the course of **multiple sclerosis** [citations omitted]." *Specification*, page 1, lines 9-14 (emphasis added). Similarly, "TNF-alpha has been found to promote development of **rheumatoid arthritis** [citation omitted]." *Specification*, page 1, lines 14-16 (emphasis added). The specification further emphasizes this similarity by listing both rheumatoid arthritis and multiple sclerosis as conditions that are promoted by increased levels of IFN-γ and/or TNF-α. *Specification*, page 3, lines 18-21; and page 6, lines 17-19. It further provides that IL-12 is known to induce TNF-α and IFN-γ. *Specification*, page 2, lines 10-11 and 22.

The specification also clearly demonstrates that inhibitors of IL-12, by reducing levels of TNF-α and IFN-γ, can significantly delay the onset and reduce the frequency of diseases that are exacerbated by these mediators. *Specification*, page 20, line 6 though page 21, line 1; and Figure 4. Given such guidance, one of skill in the art would be enabled to make and use IL-12 antagonists to treat conditions that are aggravated by TNF-α by inhibiting IL-12, such as multiple sclerosis and rheumatoid arthritis.

The specification also provides appropriate guidance as to the dosing regimens for using IL-12 antagonists--about 0.05 to about 25 mg/kg, and preferably about 0.2 to about 2 mg/kg. *Specification*, page 4, lines 4-8. And no undue experimentation would be required to determine the optimal dosing regiment of the IL-12 antagonists for any given disease. Such methodology represents only routine experimentation. Thus, the specification gives sufficient guidance to the skilled artisan to make and use IL-12 antagonists to treat rheumatoid arthritis.

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000

Finally, Applicants note that the Examiner continues to cite *Butler* in the Office Action as allegedly showing that treatment with IL-12 antibodies has no statistically significant effect on the clinical outcome of arthritis. Applicants previously questioned the statistical validity of *Butler* and continue to do so for the reasons of record. Applicants also provided the Examiner with a number of other scientific studies, which contrary to *Butler*, suggest that IL-12 antibodies would be an effective treatment for arthritis. The Examiner rejected these additional studies, though, because they were published after the filing date of the present application. As discussed with the Examiner during the recent interview, however, Butler was published even later (1999) than the some of the studies cited by Applicants. Thus, Butler cannot be relied upon to challenge enablement, while all other studies from the same time period are ignored. Applicants contend that the scientific evidence, when viewed as a whole, weighs strongly in favor of enablement and operability of this invention.

Clearly, the guidance from the specification, when taken together with the overall teachings in the art, enable one of ordinary skill in the art to make and use the present invention. Thus, Applicants respectfully request that the Examiner withdraw the rejection.

Conclusion

In view of the these amendments and remarks, Applicants respectfully request the reconsideration and reexamination of this application and the timely allowance of the pending claims. Should the Examiner not believe that the claims are in condition for allowance, Applicants request that she please contact their undersigned representative at (202) 408-4086 for an interview to discuss the application.

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: November 28, 2001

By: _____
M. Todd Rands
Reg. No. 46,249

M. Todd Rands
FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.
1300 I Street, NW
Washington, DC 20005
(202) 408-4148 (tel)
(202) 408-4400 (fax)
todd.rands@finnegan.com

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000